Overview of the HFM-181 Symposium Programme

Medical Technology Repurposed to Enhance Human Performance

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ABSTRACT

Human Performance Optimization (HPO) involves strategies to sustain performance in the face of operational stressors that degrade function (e.g., through selection, training, feeding, rest, equipping, and leadership). This differs from Human Performance Enhancement (HPE) strategies to create superhuman capabilities beyond the normal biological range through modification of human structure and function (e.g., surgery, genetic modification, pharmacology, neural stimulation, prosthetic implants). The majority of HPE opportunities arise from advances in medical research technologies to treat injury and disease where there are justifiable risk-benefit tradeoffs. The concessions in trying to improve normal human biology are different, and are typically accompanied by adverse health and performance consequences. Potential medical and HPE advances can also come from understanding biological mechanisms supporting specialized performance in other species ("bioinspired" technologies). Repurposing of medical technologies for HPE is inevitable because some athletes and others aim to be the first to employ any potential competitive advantage. The military can lead the way for ethical and thoughtful research in this area and foster a thorough understanding of both the risks and the possibilities for tactical advantages.

1.0 THE PERFORMANCE SPECTRUM: OLYMPIAN OR SUPERMAN?

1.1 Structure of the Symposium Programme

The planning committee has organized the symposium into an introduction to the optimization of human performance, followed by an exploration of human-machine interface, and then a consideration of supraphysiological enhancement of the human. The programme also includes a poster session on two specialized aspects of human performance optimization – health protection and individual health behaviors; as well as a special panel presentation and discussion on ethical considerations. Two keynote lectures feature experts on human physiological limits (Dr. Ira Jacobs) and man-machine interface (Dr. Axel Schulte). The symposium's planners are eager to promote new discussions on if and how the military should attempt to improve biological systems, and generate thoughtful assessment of the potential risks and benefits in the repurposing of new medical technologies.

1.2 Human Performance Optimization (HPO)

Human Performance Optimization (HPO) involves strategies to sustain performance in the face of operational stressors that degrade it (e.g., through selection, training, feeding, rest, equipping, and leadership). This human systems focus is often referred to as "skin-in" research in order to distinguish it from non-medical "skin-out" materiel systems. This artificial distinction has proved useful in classifying research according to the type of discipline, laboratory capabilities, and regulatory policies and procedures (1). In some armies these research responsibilities for the human and the materiel systems are separated

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between commands to ensure that primary responsibility for health and performance of the human is not inadvertently compromised in the mission to develop equipment and systems to augment capability.

1.3 Human-Systems Integration (HSI)

The boundary between “skin in” and “skin out” research becomes fuzzy in the world of Human-Systems Integration (HSI) with the advent of equipment that involves direct human operator links to engineered systems (2). Although the focus of HSI research has been on equipment and systems not on the human, but this is fast becoming an artificial distinction as we learn more about how systems may modify brain function, and evolve direct human-machine connections including implantable systems. This cultural divide between engineering and biomedical sciences includes a significant technological barrier, whereby the development of human-centric materiel must rely on inadequate research on the limits of human tolerances and underdeveloped models of health and performance data for biomedical standards. This responsibility of the medical research community continues to rank low in research priorities whenever the balance shifts to near term delivery of soldier end products, even though valid physiological models could provide leap ahead materiel solutions and save costs at every stage of development. These models and standards are needed to support materiel developers in the design of safer and more effective equipment, including personal protective equipment (e.g., ballistic protective vests, helmets, eye protection, flame retardant suits, etc.) and equipment to augment capabilities (higher powered weapons systems, nonlethal weapons systems, higher performance manned aircraft and vehicles, etc.). This becomes even more important as modern vehicles and weapons systems continue to outstrip human capabilities for maintenance-free continuous performance, tolerance of biodynamic forces (e.g., noise, acceleration, jolt), and endurance in environmental extremes (e.g., pollution, hypoxia, toxic chemicals, thermal, radiation).

1.4 Human Performance Enhancement (HPE)

Human Performance Enhancement (HPE) strategies create superhuman capabilities that go beyond the normal biological range through modification of human form and function (e.g., surgery, genetic modification, pharmacology, neural stimulation)(3). Medical research aimed at providing better treatments for injury and disease coincidentally provides these new opportunities to “improve” human biology. Safety studies required for therapeutic applications provide information on risks and side effects that might be encountered in intended medical use, but do not necessarily provide information on the adverse consequences of uses in healthy humans. As a result, HPE studies present special ethical problems because adverse effects may only emerge from long term study of normal individuals with no disease risk to weigh against the possible discovery of a tactical advantage.

1.5 What Type of Performance is Critical to Military Mission Success?

1.5.1 Minimum standards are easier to define than predictors of success

A crucial question in the discussion of HPE technologies is what capability beyond normal human capacity is useful and worth the relative risk for a gain in tactical advantage. Military performance remains poorly defined and, subsequently, needs may be changing rapidly as new technologies alter the nature of warfare. It is clear that a diversity of skills provide a team with the agility to respond to unexpected threats. After several decades of attempting to define physical characteristics essential to success in specific military occupational specialties, it has become apparent that no single attribute or measurable parameter provides a useful discriminator of who is best for a particular job (4-6). There are only minimum standards such as those used during medical inprocessing that may define some individuals who are not suited to the military (e.g., extreme underweight or overweight, preexisting medical conditions such as severe asthma, etc.).

1.5.2. Fitness and health habits will always be relevant to performance outcomes

Even minimum standards are susceptible to challenge as the military moves into a new era of information warfare. Perhaps the overweight, chain-smoking, insomniac computer hacker living in his mother's basement represents a skill set of the Army of the future! Even if the most valued skills are cognitive abilities, the connection between mind and body cannot be ignored. With the confluence of data establishing the importance of physical fitness on neurogenesis, memory capacity, and other aspects of mental resilience, the ideal soldier for today's army is still a well balanced mesomorph who strives to optimize his or her health and performance and engages in personal habits that optimize psychological, immunological, and physical resilience. This includes lifestyle such as regular exercise, no smoking or drug abuse, sleep hygiene, good nutrition, etc. These are critical aspects of human performance, and thus also one of the major themes of this symposium.

1.5.3 HPE for athletes is not necessarily useful to soldiers

The mere existence of a new approach that permits some extraordinary capability is not sufficient for adoption in the military. For example, high dose creatine supplementation provides a well established advantage to muscle strength performance (7,8); however, in military studies it provides no clear advantage (9) because muscle endurance, not a short burst of strength, is the primary performance limiter. For militarily relevant performance, other sources of fuel such as carbohydrate energy (10-12) are more important, and stimulants (e.g., caffeine, amphetamine) may also be beneficial to sustain physical and mental metabolic endurance when rest is not practical (13,14). Similarly, the list of performance-enhancing drugs banned by the International Olympic Committee is not necessarily the menu for military performance enhancement. The difference between an Olympic gold medal and no medal may be fractions of a second in speed or small differences in strength, but provide no net advantage to soldiers.

1.5.4 Extraordinary performance may exact a cost to other types of performance

Separate from health risks associated with HPE, there may also be risk to intended performance outcomes. For example, creating a massively muscled and strong supersoldier is likely to result in an individual who is less effective for other physical tasks that require endurance or flexibility, requires higher and more frequent energy intake, is more susceptible to heat strain, and so on. Another example of the risk in overemphasizing a specific trait is extreme memory performance. In the case of great capacity to remember facts, as seen in savantism, the cost may be the inability to mentalize (or because of this deficit, the compensatory mechanism of repetition provides an approach to supermemory ability)(15,16). In short, optimized humans have an expected and predictable balance of capabilities, whereas "enhanced" humans may gain extraordinary capabilities but surrender other normal capabilities.

1.5.5 Change the soldier or change the equipment?

HPE technologies must be weighed against much simpler approaches such as equipment ("skin out") solutions. Every soldier can have the capacity of the savant if provided with an iPhone or soldier computer, and this would be far easier, less risky or compromising to other performance, and immediately available. Table 1 compares potential solutions to a few examples of military performance capabilities.

Table 1. Some Examples of Operational Capabilities Classified by Category of Interventions

Performance Capability	Human Optimization (HPO)	Materiel Solution (HSI)	Human Enhancement (HPE)
Visual acuity	Squint training to temporarily modify eyeball shape	Optical devices to keep image focused on fovea	Laser corneal refractive surgery (e.g., LASIK, PRK)
Locomotion and load carriage	Science-based physical training and supplements for fuel and stamina (e.g., caffeine, carbohydrate)	Exoskeleton (e.g., Locomat)	Myostatin gene inhibition for greater mass of working muscle
Heat tolerance	Heat acclimatization training	Wearable microclimate cooling systems	Heat shock protein variant (e.g,. genetic engineering)
Protection and performance in the cold	Elevate core temperature with thermogenic supplements (e.g., ephedrine-caffeine)	Extended cold weather clothing system (ECWCS)	Enhanced brown fat storage and metabolism
Protection and work in arid environments	Trained water intake discipline; glycerol hyperhydration	Dune (“still”) suit that reclaims, filters and recycles body water losses	Enhanced renal and bladder water resorption
Altitude and underwater performance	Intermittent hypoxia training	Oxygen-generation and breathing systems	Surgically provided gills based on extracorporeal oxygen diffusion systems
Increase cognitive speed and memory	Brain training exercises (“mental gym”); olfactory linked memory activation	Soldier computer or iPhone resources	Intracortical memory chip; nanoparticle controlled release of nootropic drugs
Stress resilience	Mindfulness training; psychological coping skills	Augmented cognition system that shifts workload away from stressed team members	Genetic engineering and/or drug to moderate performance interference from limbic responses

2.0 THE MEDICAL TECHNOLOGY INVENTORY

2.1 Emerging science and engineering technology for medical treatment applications

Various science and engineering technologies that are currently being explored for medical uses are summarized in Table 2. Many of these investigations are currently in progress through the Telemedicine and Advanced Technology Research Center (TATRC) program in the U.S. Army (17). Clearly, each of these technologies can also be theoretically applied to some type of performance enhancement. Some proposed or actual HPE uses are listed.

2.2 Surgical modification

Cosmetic surgery to replace eyeglasses is becoming commonplace and the techniques are being rapidly refined with use. With wavefront-guided refractive surgery, the cornea can be sculpted to correct irregularities and to improve visual acuity better than 20/20 for young soldiers (18-20). Since the technique is still relatively new, it remains to be seen how often this surgery can be performed on the same eye before the integrity of eyeball is compromised. This is an important question for the military if young soldiers are surgically treated to eliminate the need for corrective lenses, given that accommodation and other ocular attributes are expected to change with age.

More dramatic surgical alterations can also be conceived for performance enhancement. For example, it appears that continuous alertness is possible in brains where the brainstem connection has been severed (21). Such a procedure has been performed to control epileptic seizures. This surgical procedure might provide healthy humans with an ability to rest with the unihemispheric sleep pattern of dolphins (22) that has been studied as part of the DARPA-funded program on Continuous Assisted Performance.

2.3 Pharmacological strategies

2.3.1 Drugs that enhance athletic performance

Drugs that are banned by athletic organizations because of potential unnatural performance advantages have been examined for use by the military. Anabolic drugs developed for wasting diseases (e.g., anabolic steroids) increase lean mass in normal men and have been associated with some strength gains in soldiers (23). These drugs have allowed body builders to achieve previously unparalleled increases in muscle mass, but the specific value to the military remains questionable, especially in light of unpredictable behavioural effects (24,25). Derivatives of erythropoietin are very useful in the treatment of anemias, and in healthy individuals can further increase red cell production and significantly boost aerobic performance in endurance events (26); however, there is concern that polycythemia, especially combined with dehydration during endurance performance, may produce thromboembolytic events that may have been responsible for sudden deaths in numerous European cyclists when the product first came available (27). Blood doping using autologous blood infusions was previously investigated by the US Army, but the greatest benefit was to aerobic performance of low fitness individuals and therefore of questionable value to general military performance (in lieu of better training)(28). Stimulants are among the best understood and useful drugs for military use especially in emergency conditions when sleep is not be possible (29). High dose caffeine, modafinil, and amphetamines have all been shown to be highly effective in temporarily reversing mental performance degradation in sleep deprived soldiers (13, 30-32). Amphetamine was widely used in the US military and by other armies during World War II to prevent “battle fatigue” (33). Sleep enhancers have been used by military and are highly effective in improving sleep quality and duration when soldiers have an opportunity to rest. Temazepam was used by British forces during the Falklands war (34); zolpidem is an example of sedatives currently used by US forces (35), and more precisely targeted sedatives with fewer side effects are in continuous development (36).

2.3.2 Drugs that affect mental status (“nootropics”)

Stimulants and other drugs acting on the nervous system may provide important performance improvements in patients with neurodegenerative diseases such as Parkinson’s Disease and Alzheimer’s. These drugs act to improve attention and improve memory; whereas, other drugs in this broad group reduce depression and psychological stress or act as antioxidants and vasodilators in the brain. The advanced development of an array of potentially useful performance enhancers was the subject of a conference between the U.S. DoD, Department of Veterans Affairs, and numerous industry partners in San Francisco last Fall (36). The Army investment in Parkinson’s Disease and related basic neuroscience challenges has led to many recent important breakthroughs including the discovery of the importance of

p11 protein in serious depression (37) and the relationship of such comorbid conditions to alterations in neural networks from diseases, chemical warfare insults (38), and other challenges (39). Ampakines have been investigated for memory and alertness improvement as part of a military-funded initiative on continuous assisted performance (40)(c.f., the conditions under which this class of drugs may be most useful is still being defined (41,42)). Hypocretin (orexin) is yet another promising performance sustaining intervention, having a fundamental role in sleep deprived brains, and recently also the subject of French military investigations of trypanosomiasis, a model of sleep disruption (43). Intranasal delivery of orexin has been explored as a convenient delivery system with rapid effects on brain activity (44).

2.3.2 Drug formulations and nanotechnology

Although all of these drugs have potential side effects, they are generally considered safe when used in the therapeutic range for which they were developed. Based on the experiences of the last century, we should also have discovered a new humility in appreciating how much we do not know; what appears safe and useful today is likely to be revealed as dangerous and unethical in the future. One example of increased awareness of blind spots in current pharmaceutical technology is the emerging data on epigenetic effects, where many drugs produce lasting changes on genetic expression that may even be conveyed to future generations.

While the risks associated with some performance enhancing drugs are generally well understood, their nonmedical use may present significant health risks, especially in previously untested doses and combinations. The gains provided by FDA-approved drugs repurposed to militarily-relevant performance may be questionable, especially in comparison to alternatives such as scientifically-based physical training programs, but there may be greater risk to health and performance from use of over the counter supplements available in the United States. This year, a popular sports supplement, Hydroxycut, was taken off the market after an accumulation of serious adverse effects (e.g., hepatotoxicity) and death (45). Contaminants in other supplement preparations have produced serious health effects and death - notably 37 deaths associated with a contaminated tryptophan product from genetically engineered bacteria that led to an FDA ban in 1991 (46). Other problems from combinations of products such as ephedra-based herbal preparations have also been associated with serious health consequences including death (47). A recent laboratory assay of a variety of sports supplements available to U.S. military members founds dangerous levels of contaminants such as arsenic and lead (48).

Nanotechnology and computational methods now provide for drug delivery systems with precisely designed parameters controlling timing and location of release, and rates of secretion. This was the focus of a national workshop co-sponsored by TATRC and the University of Texas Health Sciences Center in Houston in November 2007. As an example, nanoparticles can be delivered into the liver through an ingestible system and activated to release insulin at a specific glucose concentration (49). These particles can be designed with properties for optimal absorption in the intestine and retention in the liver. Such precision delivery could be designed for pharmacological enhancement of soldiers, providing prophylaxes or antidotes for neurotoxic chemicals and other battlefield threats (50).

2.4 Prosthetic devices

In the past decade, the US Army has made major investments in to prosthetic and regenerative medicine to restore functional performance of seriously injured soldiers (51). Major advances in limb prosthetics, neural interfaces to control artificial limbs and provide sensory inputs for haptic feedback, electronic retinas and intracortical implants also contribute to evolving concepts of man-machine interface, exoskeleton and other performance enhancing materiel strategies. Soldiers with modern prosthetic leg technology are returning to duty, even serving in operational environments. Based on biomechanical studies in military rehabilitation centers, Army and Navy researchers are refining the design of new powered knees based on biomechanical studies in military rehabilitation centers (52), supporting novel

concepts for better articulation of complex artificial joints such as feet (53,54) and shoulders (55), and designing proprioceptive feedback on position and forces acting on artificial feet (56). These military investments also contribute to the development of exoskeleton and other soldier performance enhancing equipment (57,58).

Electronic retina technology is advancing rapidly and can now provide limited visual capacity to the blind (59,60). This involves a retinal prosthesis that captures visual images, communicates the images to electronic interfaces with the retina, and delivers electrical pulses to the retina that create vision. One Army-supported effort is currently optimizing the electrical signals that communicate with retinal ganglion cells in the absence of photoreceptors (61). Augmented vision systems for visually impaired individuals are also being developed that have applications for military augmented vision devices and address problems of data overload that produce inattentional blindness and other problems (62). As these systems are improved, one can conceive of providing additional infrared or ultraviolet visual capabilities to humans.

Direct electrical brain interfaces have been developed with arrays of microelectrodes that penetrate the cortex, such as the Utah Electrode Array (63). Direct cortical input has been used in blind volunteers to provide visual information and is also being used in other studies to provide motor cortex control of hand and arm movements in quadriplegic patients. While these efforts are currently being developed for seriously injured soldiers, applications of the technology in healthy individuals will almost certainly be explored to counter fatigue, enhance memory, stimulate reward centers, etc. Military applications could include superhuman capabilities with reduced response time (e.g., increased speed of action in human decision making without requiring limb movement and motor action) and possibly more rapid direct data acquisition by the brain.

A major research investment in biomonitoring technologies includes investigations of host defense responses to implanted biomaterials to enhance desired responses to implants based coating properties and other local factors. Other challenges include device-tissue bonding for direct osseointegration of prosthetic limbs and skin closure around externalized devices to prevent routes of infection.

2.5 Neurostimulation

Deep brain stimulation (DBS) from electrodes implanted most typically into the subthalamic nucleus or globus pallidus is a well developed clinical tool to manage Parkinson’s tremors and other neurological symptoms that cannot be controlled with drugs. The technique has also been used in the treatment of severe depression, epilepsy, and other conditions. Adverse consequences, often associated with inadvertent stimulation of other effects and problems associated with dislocation of the electrodes, include seizure activity at frequencies outside of the therapeutic and performance enhancing range. As an alternative to implanted electrode, transcranial magnetic stimulation (TMS) is being investigated in military programs as a non invasive treatment of Parkinson’s Disease, with brief exposures to an external electromagnetic field providing longterm relief of tremors (64). This has also been investigated in a DARPA program to restore performance in fatigued individuals following frontal lobe exposure (65, 66).

Vagal nerve stimulators have been used in patients to control epilepsy with intermittent stimulation of the vagus nerve inhibiting seizure activity (67). Other investigations suggest that this may also provide specific mental performance benefits such as enhanced memory formation when administered after learning (68).

2.6 Genetic engineering

Gene therapy is becoming an accepted technology especially where any experimental risks are considered well worth the alternative of the consequences of a devastating neurodegenerative disease. One approach

involves altering the expression of an enzyme by introducing genes with a viral vector. This is being explored to treat comorbid symptoms in Parkinson's Disease by introducing glutamic acid decarboxylase in affected brain regions (69). Another example military application, paroxonase gene polymorphisms explain some variability in susceptibility to both cardiovascular disease and organophosphate poisoning (70, 71) as well as dementia and brain tumors (72, 73). Expression of the PON1 gene is increased by other approaches such as use of simvastatin (74) but could also be delivered by genetic engineering.
Other treatments, especically where a single gene defect provides the cure for a disease such as Huntington's may become common cures in the near future. Likewise, simple single mutations such as a defect in the myostatin gene produces massively muscled and lean blue cattle, and similar defects in the expression of myostatin protein have been identified in as a mistake of nature (75, 76) could be used to produce massive muscled individuals, if this is deemed important to the Army. This is an important prospective treatment for muscular dystrophy and for old age sarcopenia, where deficiency states exist. The physiological lessons may be learned for normal athletes who will flock to this, addressing questions such as do we deplete satellite cells and possibly produce sarcopenia later in life, what are the limits to muscle size relative to tendons and bone before tendon ruptures and broken bones occur. Likewise, it can already be predicted that these individuals will be special risks for heat injury because of the extraordinary mass to surface area ratio that hampers thermoregulatory ability.

Genetic "experiments of nature" such as the dysfunctional regulation of myostatin may lead to genetic manipulation or, with further understanding, lead to specific drugs with more controllable or even temporary effects. Congenital analgesia is a trait linked to mutation in the SCN9A gene that can produce an inability to sense physical pain (77). This rare condition in children is potentially dangerous but a duplication of the effect could be hugely advantageous to a soldier who must continue a mission in the face of painful injuries or other external stimuli. Battlefield pain management is a high priority in military medical research; some of these solutions will certainly find their way into extending human performance.

2.7 Stem cells and regenerative medicine

Major research initiatives in regenerative medicine launched by the US Army have focused on repair and restoration of tissues, organs, and entire sections of composite tissues. Two large research consortia that are focused on producing early advances for treatment of injured servicemembers in burn repair, wound healing without scarring, craniofacial reconstruction, and compartment syndrome (Armed Forces Institute of Regenerative Medicine, AFIRM). Other Army initiatives and projects include nanoscaffolding to regrow injured nerve axons in peripheral nerve injury, regrowth of major muscle damage including cardiac tissue or skeletal muscle, reconstruction of major blood vessels, and extensive bone repair models. In a planned succession of medical technologies, current advances in prosthetic limb technology will give way to routine heterologous limb transplants (as immune responses are successfully managed)(78), and these will eventually be replaced with regenerative techniques to restore ones own tissues.

Adult stem cells have been recovered from fat tissue and used to coat the lumen of synthetic vessel to create biological intraluminal linings. Stem cells are being investigated for repair of damaged tissues, with strategies to enhance the chemotactic responses from damaged tissues to precisely position the needed cells. The same stem cell methods could form the basis of HPE technologies of the future used to mitigate trauma-induced inflammation and to provide supportive therapy to sustain soldier function to continue the mission (79-81). Mesenchymal stem cells may promote wound healing in general (82) and there already exists an off the shelf product being tested in hematopoetic stem cell transplantation.

Table 2. Science and Engineering Technologies with Medical and Potential HPE Applications

Technology	Example Applications in Medicine	Example "Repurposing" to performance capability
Surgery	▪ surgical ablation of brain tissue for epilepsy ▪ surgical sectioning through the corpus collosum for epilepsy	▪ Corneal laser refractive surgery ▪ Surgical sectioning to allow unihemispheric sleep and continuous alertness
Pharmacology	▪ narcolepsy (modafinil) ▪ treatment of sarcopenia and osteoporosis (anabolic steroids) ▪ memory enhancers for dementia (Aricept) ▪ treatment of anemia (recombinant erythropoietin)	▪ Delayed need for sleep - nootropics ▪ Enhanced memory capability (Provigil, Aricept, Ritalin) ▪ Produce huge muscle mass ▪ Creation of "human llamas" with altered oxygen carrying capacity ▪ Prophylactic "smart" nanoparticle drugs for precision release if needed
Prosthetic devices	▪ cardiac pacemakers ▪ osteointegrated artificial limbs ▪ neurally controlled limbs ▪ electronic retinas ▪ intraocular lens implants ▪ cochlear implants ▪ intracranial implants ▪ artificial pancreas (closed loop system)	▪ Prosthetic limbs that provide superhuman strength and endurance ▪ Ocular prostheses for infrared, ultraviolet and other nonhuman visual capabilities ▪ Auditory systems that provide specific/filterable and ultrasensitive hearing capacity
Neurostimulation	▪ Intracranial implants ▪ Vagal stimulators for depression ▪ Transcranial magnetic stimulation for depression and epilepsy	▪ Vagal stimulation to counter stress responses ▪ Transcranial magnetic stimulation of frontal lobes to counter fatigue
Genetic engineering	▪ overexpression of neurotrophic factors in neural cells transduced by viral vector delivery or genetically modified cell implants for Huntington's Disease, Parkinson's Disease, and type 1 diabetes	▪ Manipulation of myostatin gene to enhance muscle mass ▪ Overexpression of PON1 gene to accelerate inactivation of nerve agent in a threat environment ▪ Reduced pain sensation (SCN9A)
Stem cell therapy and regenerative medicine	▪ bone marrow replacement ▪ corneal repair ▪ tendon-bone repair ▪ spinal cord injury	▪ Rapid repair and sustainment following normally incapacitating injuries ▪ Enhanced brain capacity?

3.0 BIO-INSPIRED HUMAN PERFORMANCE ENHANCEMENT

3.1 Biological performance currently outside of the bounds of the human species

HPE opportunities may also be derived from an understanding of biological mechanisms that exist elsewhere in nature. As an example of applications to medicine, deer antler regeneration provides a mammalian model for understanding the hormonal triggers for pluripotent stem cell regeneration of a complex structure. Deer antler biology also suggests strategies for cell-metal interface to prevent the infections around external implants, such as osseointegration of prosthetic legs. Hibernators such as bears and ground squirrels are being studied in TATRC-supported research for the biochemical adaptations that preserve tissues in a hypoxic environment such as damaged ischemic heart muscle (83, 84). This same hibernation research may provide effective strategies to preferentially burn fat in weight reduction (85).

3.2 Bio-inspired opportunities for human performance

There are many interesting possibilities for humans to be enhanced either with devices based on animal adaptations or even with genetic engineering of other superhuman capabilities. Some examples of potentially useful capabilities are shown in Table 3. DARPA-supported research has investigated mechanisms that may enhance human performance, including long range continuous flying of migrating birds and the ability to sleep only one portion of the brain at a time in dolphin unihemispheric sleep (22). The hibernation studies on bears and ground squirrels may lead to strategies for tolerance in temperature extremes and improve recycling of bone mineral and urea to meet extreme operational requirements.

Adoption of any of these specializations for human performance enhancement is likely to come at a cost of more generalized capabilities. For example, “human llamas” with left-shifted dissociation curves may have excellent advantages at altitude but will be disadvantaged at sea level. Likewise, sprinters have a very different muscle metabolic profile than distance runners, with differences in glycolytic enzyme activity, and cross sectional area of fast twitch muscles; the best soldiers may be the most well rounded, with a variety of capabilities to meet unexpected threats with greater agility. Ultimately, we may learn the most from the physiological resilience of rats, one of the most successful mammals that has penetrated virtually every environmental niche occupied by humans. Rats have generalized rather than specialized, so that they can handle a wide variety of threats through quick learning and behavioural adaptation.

3.3 Materiel solutions to assist human performance

Nonmedical applications of bio-inspired engineering and computing technologies are a recognized priority in basic research for the Army, and a major program with this focus was funded at the Institute of Creative Biotechnologies (86). Specialized uses of unique proteins (e.g., rhodopsin for energy production from sunlight) and new computational approaches such as swarm intelligence, evolutionary algorithms, and ant colony optimization are examples of such biologically-inspired technology. Artificial nose technologies were originally funded by the Navy to detect petroleum products in the water leaked by diesel submarines (87, 88). The synthetic nose technology was expanded in a DARPA project to artificial monitoring of smell “fingerprints” related to HLA expression, just as a blood hound can follow an individual’s unique scent (89). Although it might be convenient for soldiers to have the olfactory sensitivity of a bloodhound, reverse engineering to create helpful devices rather than engineering modification of the human is usually an easier and safer solution. Many useful devices are yet to be developed based on nature’s solutions; for example, a platypus-like electromagnetic sensor might help detect opponents hidden with from detection by physiological cloaking of heat and other signatures (90). There is also a long history of useful medical products discovered in other species such as hirudin in leeches and epibatidine in poison arrow frogs.

Table 3. Some Extraordinary Biological Capabilities in Nonhuman Species

Capability	Species	Mechanism
Limb regeneration	Axolotl (***Ambystoma mexicanum***)	Recapitulate embryogenesis
Dehydration tolerance to >30% of body weight	Camels (***Camelus dromedarius***)	Efficiencies in water expenditure, including insensible water loss, and red cell stability at high osmolarity
Suspended animation	Brown Bears (***Ursus arctos***)	Hibernation with only slight hypothermia; recycling of bone mineral and urea; ischemic protection
Freezing injury protection during subzero body cooling	Arctic Ground Squirrels (***Spermophilus parryii***)	Supercooling without antifreeze proteins
Unihemispheric sleep for continuous operations (CONOPS)	Bottlenosed Dophins (***Tursiops truncatus***)	NonREM sleep switches between left and right brain to maintain vigilance while part of the brain sleeps
Detection of prey by olfactory acuity	Blood hound (***Canis familiarus***)	High density of olfactory receptor cells (4 billion in 59 sq inches of olfactory surface area)
Detection of prey by electroreceptor sensing of muscular contractions	Duckbilled Platypus (***Ornithorhynchus anatinus***)	Electroreceptor organs that can detect muscle activity of underwater prey
Running speed up to 70 mph	African Cheetah (***Acinonyx jubatus***)	Biochemical and physiological specialization for anerobically based performance for sprinting
High altitude aerobic capacity	Llama (***Llama glama***)	Left-shifted oxyhemoglobin dissociation curve and more efficient tissue O2 extraction
Breath holding for up to >800 m water depth and for up to 48 minutes	Northern Elephant Seals (***Mirounga angustirostris***)	Hypoxic tolerance with vascular shunting to brain and heart; extreme reduction in heart rate
Complex communications capabilities	Killer Whale (***Orcinus orcus***)	Extreme development of cortex, especially temporal & insular regions
Visual hyperacuity	African Serpent Eagle (***Dryotriorchis spectabilis***)	Visual resolution greater than 2x of human acuity with greater cone density in the retina
Survival in extreme and toxic environments	Extremophiles (e.g., ***Deinococcus radiodurans)***	Biochemical detoxification of heavy metals, radionuclides etc.

4.0 SOLDIER OF THE FUTURE: ACCESSORIZED OR BIOLOGICALLY ENHANCED?

4.1 How do we compare to Superman?

How do humans compare to Superman and to other species? In the animal kingdom, humans are distinguished more for their brain development and learning ability than for any other specialized trait or capability. Our brain is central to what makes us human. A Superman with completely unworldly brain function might not have received such a sympathetic readership. Although he had other specialized skills such as x-ray vision and superhearing, Superman had three famous claims, listed in Table 4 with comparison to human skills, and specialized animal skills. Man is not extraordinarily fast, and can only achieve speeds of 25 mph compared to cheetahs that can produce bursts of up to 70 mph and some birds (e.g., swifts, peregrine falcons) can exceed 100 mph. Man is also not so powerful, lacking mass and strength of some other animals. Man also cannot jump as impressively as the standing leaps of some other animals. In each of these cases, however, man has been able to design “skin out” personal equipment systems that do not require any redesign of the human to meet some of the Superman capabilities. Exoskeleton concepts and backpack jet engines are two examples of such technology (91).

Computers may never surpass biological brains, and higher performance computing might actually be based on “wet ware” composed of neural cell networks. The field of network science is heavily invested in bio-inspired strategies. Conceivably, human brains could even be yoked into a collective of massively parallel computing, as imagined for the “Borg” in the science fiction program Star Trek.

Table 4. What Can Superman Do and How Do We Compare, without a Jetpack and Exoskeleton?

• **Faster than a Speeding Bullet** (1000 m/s)
swifts and peregrine falcon >40 m/s; cheetah 29 m/s; orca 15 m/s; man >10 m/s (fastest man: Usain Bolt 9.69 s in the 100 m sprint)
• **More powerful than a locomotive** (gas turbine electric 4,000 HP (3,000 kW))
blue whale 500 HP?; elephant 4-5HP?; human ~2 HP (1500 W)
• **Able to Leap Tall Buildings in a Single Bound** (Empire State building 381 m (1250 ft))
some cats such as the cougar, 18 ft high; red kangaroo 10 ft; human 2.45 m (high jump record: Javier Sotomayor)

4.2 What intrinsic superhuman capability do we really need for the Soldier of 2050?

Physical fitness, nutrition, and rest will be scientifically based and personalized to optimize the individual based on their existing genetic profile. With a new focus on information technology warfare, the soldier’s mental capacity will be the most valued outcome, including everything from psychosocial aspects such as leadership, interpersonal relations, and unit cohesion to cognitive functions such as memory, planning, and decision making. Psychological resilience will also help to regulate overall physiological resilience, perhaps trained using techniques from Buddhist and other religious teachings and with a recognized neuroscience basis (92). Genetics will identify strengths and vulnerabilities of individuals so that they can be classified to take advantage of their most important capabilities and medically monitored and prepared or protected against injury and other hazards based on identified vulnerabilities. Further advances on man-machine interface will greatly improve the value of equipment and vehicles, with brain signals instantaneously and correctly evoking equipment responses, and computers distributing workload based

on operator performance and mental status (93, 94). Biomonitoring technologies will allow each individual to push to individual human limits without fatigue and injury (95).

4.3 What will we miss about Soldier 2010?

The brain of Soldier 2050 will be substantially different, changed by new modes of communication and social interactions. Nonverbal communications to include olfactory signals, body language, visual cues may be gone. The still poorly understood olfactory signals such as androsterone secretion and oxytocin that have such profound effects on behaviour (96) will no longer contribute to the rich pastiche of subtle signals that make up human communication. There may less mirror neuron-mediated learning and social cues, and the entire force may act without emotional and human context in an Asperger's syndrome-like world. A new brutal honesty will be pervasive, with no thought unexpressed through incessant twitter-like communications and perhaps extending to virtual "mind melds" for high volume information exchange.

It is even possible that the soldier best equipped for information age warfare is the overweight poorly conditioned insomniac computer hacker geek living in his mother's basement. This will be a very different Army. Perhaps this on an evolutionary trajectory that leads to "navigators" with highly evolved brains described by Frank Herbert in his book "Dune" (97). In the 1985 David Lynch movie version, these were massive disembodied and all-knowing brains, with full time attendants to sustain them floating in their individual media and serving as communication conduits to the world. We are already able to sustain individuals who have awareness and intact brains in bodies that are losing function. Limited interactions to the outside world such as eyeblinks is now being enhanced by new neurotechnologies.

5.0 CONCLUSION

What we want to enhance in soldiers is resilience and agility to operate against any threat, with a human sensitivity that allows social and humane interactions but also an ability to separate from and remain calm in a traumatic and potentially emotional situation to prevent over-responses that produce bad decisions and may result in later pathology. We can immediately do a great deal more to optimize the human in operational environments through HPO strategies and with sophisticated equipment tightly interfaced to operators. It will still be important to retain the element of surprise with unexpected, seemingly irrational solutions to a threat that wins the day over the computed solution. Thus, optimization of the individual is not the same as homogenization with the textbook/computed answer. The best soldier will be a coherent healthy optimized individual who does not engage in health harmful behaviours. As the head belongs on the body, physical optimization contributes to mental performance optimization in many important ways that we are just beginning to understand in the neurobiology of exercise (improved memory and learning capacity; increased protection against psychological stressors; resilience against pain syndromes such as fibromyalgia; etc.). Protective equipment surrounding the soldier can provide extraordinary capabilities to operate in extreme environments with microclimate cooling, toxic inhalation protection, water recycling, etc. Most important in this era of information science are the training and materiel technologies for information handling that assist the well educated, learning-enabled, and trained soldier.

We are not likely to substantially improve our biology without encountering second order consequences from tampering with the finely balanced physiological web. Eventually, a comprehensive model of the genetically coded physiology of every plant and animal species will provide a remarkable understanding of what is possible in existing biological mechanisms and how various combinations of attributes might function together in a viable mutant. By fully understanding the advantages and disadvantages of new medical technologies and what may be possible, we will avoid technological surprise and can better understand the vulnerabilities of any opponent choosing to use medical technologies for HPE.

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